

# Drug Metabolism and Disposition:

## the biological fate of chemicals

March 1995

Vol. 23, No. 3

### CONTENTS

#### ACCELERATED COMMUNICATION

Expressed Human UGT1.4 Protein Catalyzes the Formation of Quaternary Ammonium-linked Glucuronides. MITCHELL D. GREEN, WARREN P. BISHOP, AND THOMAS R. TEPHLY . . . . . 299

#### ARTICLES

Sulfation and Glucuronidation of Acetaminophen by Human Hepatocytes Cultured on Matrigel and Type 1 Collagen Reproduces Conjugation *in Vivo*. ROBERT E. KANE, ALBERT P. LI, AND DONALD R. KAMINSKI . . . . . 303

Comparative Metabolism of 3'-Azido-3'-deoxythymidine in Cultured Hepatocytes from Rats, Dogs, Monkeys, and Humans. FLORENCE NICOLAS, GEORGES DE SOUSA, PASCAL THOMAS, MICHEL PLACIDI, GIOCONDO LORENZON, AND ROGER RAHMANI . . . . . 308

Effect of Iron Overload on the Metabolism and Urinary Recovery of 3-Hydroxypyridin-4-one Chelating Agents in the Rat. RUKSANA CHOUDHURY AND SURINDER SINGH . . . . . 314

Human Liver Cytochrome P4503A Biotransformation of the Cyclosporin Derivative SDZ IMM 125. ALISON E. M. VICKERS, ERIN MEYER, ROBERT DANNECKER, BLANDINE KELLER, RONALD E. TYNES, AND GERARD MAURER . . . . . 321

Sites of Biotransformation for the Cyclosporin Derivative SDZ IMM 125 Using Human Liver and Kidney Slices and Intestine: Comparison with Rat Liver Slices and Cyclosporin A Metabolism. ALISON E. M. VICKERS, ROBYN L. FISHER, KLAUS BRENDL, JOSEPH GUERTLER, ROBERT DANNECKER, BLANDINE KELLER, AND VOLKER FISCHER . . . . . 327

Comparative Disposition of Morphine-3-glucuronide during Separate Intravenous Infusions of Morphine and Morphine-3-glucuronide in Sheep: Importance of the Kidney. ROBERT W. MILNE, COLIN F. MCLEAN, LAURENCE E. MATHER, ROGER L. NATION, WILLIAM B. RUNCIMAN, ALBERT J. RUTTEN, AND ANDREW A. SOMOGYI. . . . . 334

Characterization of the *in Vitro* Glucuronidation of Flurbiprofen Enantiomers. MOHAMED HAMDOUNE, JACQUES MOUNIE, JACQUES MAGDALOU, TAOUFIK MASMOUDI, HERVÉ GOUDONNET, AND ANDRÉ ESCOUSSE . . . . . 343

*In Vivo* Disposition of Caffeine Predicted from Hepatic Microsomal and Hepatocyte Data. KAREN A. HAYES, BEVERLEY BRENNAN, RICHARD CHENERY, AND J. BRIAN HOUSTON . . . . . 349

Reduction of the Prodrug Loperamide Oxide to Its Active Drug Loperamide in the Gut of Rats, Dogs, and Humans. KAREL LAVRIJSEN, DIRK VAN DYCK, JOS VAN HOUDT, JAN HENDRICKX, JOHAN MONBALIU, ROBERT WOESTENBORGH, WILLEM MEULDERMANS, AND JOS HEYKANTS. . . . . 354

Metabolism and Elimination of 5,6-Dimethylxanthone-4-acetic Acid in the Isolated Perfused Rat Liver. LORRAINE K. WEBSTER, ANDREW G. ELLIS, PHILIP KESTELL, AND GORDON W. REWCASTLE . . . 363

Reactivity of Tolmetin Glucuronide with Human Serum Albumin: Identification of Binding Sites and Mechanisms of Reaction by Tandem Mass Spectrometry. ANDREAS DING, PARNIAN ZIA-AMIRHOSSEINI, ANTONY F. McDONAGH, ALMA L. BURLINGAME, AND LESLIE Z. BENET . . . . . 369

Identification of Tamoxifen Metabolites in Human HEP G2 Cell Line, Human Liver Homogenate, and Patients on Long-term Therapy for Breast Cancer. G. K. POON, B. WALTER, P. E. LØNNING, M. N. HORTON, AND R. MCCAGUE . . . . . 377

*Continued on next page*

Contents (cont'd.)

<i>In Vitro</i> Metabolism of Tirilazad Mesylate in Male and Female Rats: Contribution of Cytochrome P4502C11 and $\Delta^4$ -5 $\alpha$ -Reductase. LARRY C. WIENKERS, RICK C. STEENWYK, STEVEN A. MIZSAK, AND PAUL G. PEARSON . . . . .	383
Kinetics of Drug Metabolism in Rat Liver Slices: Rates of Oxidation of Ethoxycoumarin and Tolbutamide, Examples of High- and Low-Clearance Compounds. PHILIP D. WORBOYS, ALAN BRADBURY, AND J. BRIAN HOUSTON . . . . .	393
Thiopurine Methyltransferase Pharmacogenetics: Cloning of Human Liver cDNA and a Processed Pseudogene on Human Chromosome 18q21.1. DANIEL LEE, CAROL SZUMLANSKI, JON HOUTMAN, RONALD HONCHEL, KATHERINE ROJAS, JOAN OVERHAUSER, ERIC D. WIEBEN, AND RICHARD M. WEINSHILBOUM . . . . .	398
<i>N</i> <sub>4</sub> -Hydroxylation of Sulfamethoxazole by Cytochrome P450 of the Cytochrome P4502C Subfamily and Reduction of Sulfamethoxazole Hydroxylamine in Human and Rat Hepatic Microsomes. ALASTAIR E. CRIBB, STEPHEN P. SPIELBERG, AND GEARÓID P. GRIFFIN . . . . .	406
Comparative Analysis of Cytochrome P4503A Induction in Primary Cultures of Rat, Rabbit, and Human Hepatocytes. THOMAS A. KOCAREK, ERIN G. SCHUETZ, STEPHEN C. STROM, ROBERT A. FISHER, AND PHILIP S. GUZELIAN . . . . .	415
Biliary Excretion of Pyrrolic Metabolites of [ <sup>14</sup> C]Monocrotaline in the Rat. MICHAEL W. LAMÉ, A. DANIEL JONES, DEXTER MORIN, H. J. SEGALL, AND DENNIS W. WILSON . . . . .	422

SHORT COMMUNICATIONS

Induction of Catechol- <i>O</i> -methyltransferase in the Luminal Epithelium of Rat Uterus by Progesterone: Inhibition by RU-486. KATSUHIRO INOUE AND CYRUS R. CREVELING . . . . .	430
Formation of Chloroethylamine and 1,3-Oxazolidine-2-one following Ifosfamide Administration in Humans. M. S. HIGHLEY, G. MOMERENCY, K. VAN CAUWENBERGHE, A. T. VAN OOSTEROM, E. A. DE BRUIJN, R. A. A. MAES, P. BLAKE, J. MANSI, AND P. G. HARPER . . . . .	433
Selectivity of Cytochrome P4502E1 in Chlorzoxazone 6-Hydroxylation. HIROSHI YAMAZAKI, ZUYO GUO, AND F. PETER GUENGERICH . . . . .	438

Erratum

Kenneth S. Lown, Joseph C. Kolars, Kenneth E. Thummel, Jeffrey L. Barnett, Kent L. Kunze, Steven A. Wrighton, and Paul B. Watkins: Interpatient heterogeneity in expression of CYP3A4 and CYP3A5 in small bowel: lack of prediction by the erythromycin breath test. *Drug Metab. Dispos.* 22, 947-955 (1994).

The units for 1'-hydroxy midazolam formation rates listed throughout the text and figures should be pM/min and not pg/min as given.

ANNOUNCEMENT

The 14th International Symposium of the Society of Toxicologic Pathologists will be held from June 11 to 15, 1995 at the San Diego Marriott Hotel and Marina, San Diego, California

For information, contact Mary M. O'Connor, Society of Toxicologic Pathologists, 875 Kings Highway, Suite 200, Woodbury, NJ 08096-3172. Phone: (609) 845-1720. Fax: (609) 853-0411. Deadline for abstract submissions is April 7, 1995.